I U C L I D

Data Set

Existing Chemical	:	ID: 68515-75-3
EINECS Name	:	Hexanedioic acid, di-C7-9-branched and linear alkyl esters
Generic name	:	Di(C7-9-alkyl) adipate
CAS No.	:	68515-75-3
EC No.	:	271-105-9
Tag name	:	SANTICIZER 97

Producer related part

Company	:	Solutia Inc.
Creation date	:	30.04.2001

Substance related part

Company	:	Solutia Inc.
Creation date	:	30.04.2001

Status	:	
Memo	:	
Printing date	:	09.06.2003
Revision date	:	30.04.2001
Date of last update	:	09.06.2003
Number of pages	:	25
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

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1.1.0 SUBSTANCE IDENTIFICATION

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2.1 MELTING POINT

Value	:	-79 - °C
Sublimation	:	
Method	:	other: measured
Year	:	2001
GLP	:	no data
Test substance	:	other TS
Test substance	:	Reported for surrogate Dioctyl Adipate [CAS No. 103-23-1).
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

29.05.2003 (1)

2.2 BOILING POINT

Value	:	355 - °C at hPa
Decomposition	:	
Method	:	other:Antoine Equation calculation
Year	:	1982
GLP	:	no data
Test substance	:	other TS
Test substance	:	97 Adipate [CAS no. 68515-75-3]
Reliability	:	(2) valid with restrictions Solutia in-house calculation study using Antoine Equation, as follows: log VP (mm Hg)= 10.0778-4519.8/T.
Flag	:	Critical study for SIDS endpoint

29.05.2003 (2)

2.3 DENSITY

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value	:	0.00001085 hPa at 25 °C
Decomposition	:	
Method	:	other (calculated)
Year	:	1982
GLP	:	no data
Test substance	:	other TS
Method	:	Solutia in-house calculation study conducted using Antoine Equation of log VP (mm Hg) = 10.0778 - 4519.8/T.
Result	:	Other values: 4.4 hPa @ 200 degrees C; 36 hPA @ 250 degrees C.
Test substance	:	97 Adipate [CAS No. 68515-75-3]
Reliability	:	(2) valid with restrictions Data consistent with other values measured at temperatures above and below the temp. used in this study
Flag	:	Critical study for SIDS endpoint

29.05.2003 (2)

2.5 PARTITION COEFFICIENT

Partition coefficient	:	
Log pow	:	> 6.48 - at °C
pH value	:	-
Method	:	other (measured)
Year	:	1980
GLP	:	no data
Test substance	:	other TS
Method	:	Used purified octanol (extracted 2X with H2SO4 and NaOH) and twice distilled deionized water. Four concentrations (110, 150, 1100 and 1200 ppm) of 97 Adipate in octanol were evaluated. The amount of 97 Adipate remaining in the octanol was determined by diluting the octanol with isooctane containing methyl stearate internal standard followed by GC/MS analysis. Level of detection was 5 ppb.
Result	:	After centrifuging the water to completely separate the phases, the average concentration in all the waters was less than the lowest level of detection (< 5 ppb). Using this level a calculated lower limit for P was determined as >2.2 X 10E5 and a corresponding BCF calculated to be > 1000 using the method of Neely et al 1974. Environ Sci Technol 8:1113.
Test substance	:	97 Adipate [CAS No. 68515-75-3]
Reliability	:	(2) valid with restrictions Method consistent with OECD guidance and well documented.
Flag	:	Critical study for SIDS endpoint

18.11.2002 (3)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	
Value	:	< .048 - mg/l at 25 °C
pH value	:	-
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	other
Year	:	1982
GLP	:	yes
Test substance	:	other TS
Method	:	Saturator column technique used. A level of 5% 97 Adipate was coated on a 100 mesh Chromosorb WHP column, then loaded into a saturator column. Vials of eluent were collected, each containing isooctane with methyl stearate as an internal standard. Four vials were taken during a flow rate of 5 ml/m and 4 at a flow rate of 2.5 ml/m. 97 Adipate was measured by GC/MS using a level of 48 ppb as the limit of detection.
Result	:	A total of 8 samples were taken and analyzed, with no detectable 97 Adipate found in any sample. Hence, the water solubility was considered less than 48 ppb, the limit of detection in this assay.
Test substance	:	97 Adipate, Technical grade of 99% purity.
Reliability	:	(2) valid with restrictions Method consistent with OECD guidance and well documented.
Flag	:	Critical study for SIDS endpoint

24.10.2002 (4)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Type	:	water
Light source	:	Sun light
Light spectrum	:	- nm
Relative intensity	:	- based on intensity of sunlight
DIRECT PHOTOLYSIS		
Halflife t1/2	:	-
Degradation	:	0 - % after 14 day(s)
Quantum yield	:	
Deg. product	:	
Method	:	other (measured)
Year	:	1981
GLP	:	yes
Test substance	:	other TS
Method	:	Used sunlight photolysis screening method following ASTM E47.06 guidance, whereby 97 Adipate was added to quartz tubes containing either purified water or membrane-filtered river water and held either in darkness or in a combination of sunlight (14 hr) and darkness (10 hr), 24 hr/day for up to 14 days. A 0.107 g/100 ml 97 Adipate stock solution was made in acetonitrile; then 100 ul of a 10:100 ml dilution was injected into quartz tubes containing 10 ml of either membrane-filtered, purified water or membrane-filtered river water. A total of 20 tubes were prepared, with 4 tubes analyzed at time 0, and two tubes containing each type of water with test material that were analyzed after 2, 5, 9 and 14 days of testing. The ave. low temp. during this study was 64 degrees F. and the high ave. was 81 degrees F. Each test vial was extracted with isooctane and analyzed for test material by GC/MS. Due to initial results obtained, a stability experiment was also conducted in a similar pattern as before, except triplicate tubes were extracted immediately after spiking, after refrigeration and after sterilization with formaldehyde.
Result	:	Initial studies indicated rapid loss in both samples, those exposed to sunlight as well as those exposed to complete darkness; the T1/2 of samples exposed to darkness were equal to or less than those exposed to sunlight. These data suggested that phenomenon other than direct photolysis or chemical transformation was occurring. For this reason the stability study was conducted. Results of the stability study confirmed that no detectable photolytic or chemical transformation occurs after the addition of 97 Adipate and the loss observed in the initial studies were the result of biodegradation from contamination of bacteria in the test system.
Test substance	:	Technical grade 97 Adipate, 99% pure.
Reliability	:	(2) valid with restrictions In-house study with good documentation.
Flag	:	Critical study for SIDS endpoint

29.05.2003 (5)

Type	:	other
Light source	:	
Light spectrum	:	- nm
Relative intensity	:	- based on intensity of sunlight
Method	:	Used AOPWIN. Version 190. an estimation model recommended by US EPA.
Remark	:	Direct photolysis in water or water droplets occurs when a photon is absorbed by a compound, which leads to the formation of an excited form, which in turn can react in a variety of ways to form more stable products. Only a small portion of synthetic organics absorb UV light above 295 nm, the sunlight region of the spectrum.. Absorbance of sunlight in this range is needed for a compound to undergo direct photolysis. Aliphatic and

needed for a compound to undergo direct photolysis. Aliphatic and oxygenated compounds including acids and that do not contain polycyclic aromatics or polyhalogenated aromatics absorb only below 220 nm and would not be considered able to directly photolyze.Thus, 97 Adipate is not expected to absorb UV light at 295 nm or higher.

Result : Vapor phase 97 Adipate is susceptible to reaction with photochemically produced hydroxyl radicals. The 2nd order rate constant for reaction with hydroxyl radicals was calculated as 23.8037E-12 cm3/(molecule*sec). Based on 1.5E6 HO molecules/cm3 and assuming 12 hrs of sunlight per day, the estimated photo-oxidation half-life is 10.8 hr.

Test substance : 97 Adipate [CAS no. 68515-75-3].

Reliability : (2) valid with restrictions

09.06.2003 (6)

3.1.2 STABILITY IN WATER

Deg. product :

Method : other (calculated)

Year : 2002

GLP : no

Test substance : no data

Method : Calculated estimates from HYDROWIN, ver. 1.67.

Result : Half-life estimated to be 3.215 yr. Hydrolysis is slow at neutral pH and breaks down to mono ester and free alcohol.

Test substance : 97 Adipate [CAS No. 68515-75-3].

Reliability : (2) valid with restrictions
Model used to estimate hydrolysis is recommended by US EPA for this purpose. Actual conduct of an OECD Guideline # 111 Hydrolysis study for this material is considered impractical, due to the extreme water insolubility of 97 Adipate. The water solubilty value of <0.048 mg/L is based on use of analytical methods whereby 48ppb was the detection limit attained in that study. No 97 Adipate was actually detected, thus the "less than" characterization of that limit. Test Guidelines stipulate that test substances should be soluble at a level of at least 20 mM in order to conduct a guideline 111 study. The value of < 0.48 ppb level for 97 Adipate is equivalent to 0.13 mMol. (based on Mol. Wt. of 356.55 g/Mol.) and is thus below the guideline limit.

Flag : Critical study for SIDS endpoint

29.05.2003 (7)

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type : fugacity model level III

Media :

Air : .278 % (Fugacity Model Level I)

Water : 3.61 % (Fugacity Model Level I)

Soil : 27.3 % (Fugacity Model Level I)

Biota	:	% (Fugacity Model Level II/III)
Soil	:	68.8 % (Fugacity Model Level II/III)
Method	:	other
Year	:	2002
Method	:	Calculated using estimated values according to Mackay, Level III. Assumed emissions (1000 kg/hr) to air, water and soil compartments using following data inputs: Henry's LC=1.81e-005 atm-m3/mole (Henrywin program), Vapor Press=6.67e-005 mm Hg (Mpbpwin program), Liquid VP=7.46e-005 mm Hg (super-cooled), Melting Pt=29.9 deg C (Kowwin program) and Soil Koc=1.45e+007 (calc by model). Last soil entry included data estimate for sediments.
Test substance	:	97 Adipate [CAS No. 68515-75-3].
Reliability	:	(2) valid with restrictions Estimated values based on model recommended by US EPA.
Flag	:	Critical study for SIDS endpoint

29.05.2003 (7)

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type	:	aerobic
Inoculum	:	
Contact time	:	
Degradation	:	67 - 88 (±) % after 24 hour(s)
Result	:	inherently biodegradable
Deg. product	:	
Method	:	OECD Guide-line 302 A "Inherent Biodegradability: Modified SCAS Test"
Year	:	1976
GLP	:	no
Test substance	:	other TS
Method	:	Two different measures of biodegradability were determined; 1) primary biodegradability measuring the disappearance of the analytical response for the original material was determined using the Semi-Continuous Activated Sludge (SCAS) technique, and 2) ultimate biodegradability, or conversion of the material to carbon dioxide, water, inorganic salts and normal metabolic products, was determined by carbon dioxide evolution procedures. The SCAS methodology followed that reported in J. Am Oil Chem Soc 46:432-440, a methodology consistent, but a predecessor of OECD test guideline 302. Test material was added to activated sludge obtained from a local domestic sewage treatment plant in 1.5 L glass vessels which were stirred magnetically at a level of 5 and 20 mg/24 hr. After a 3 week acclimation period, primary degradation was determined each week by analyzing 50-ml liquor samples withdrawn after feeding and at the end of the aeration cycle. Analysis was made using a GC with a FID detector. A blank unit was maintained on synthetic sewage without the addition of any test material. The Carbon dioxide Evolution test followed the procedures as outlined by Sturm (J. AM Oil Chem. Soc. 50:159-167, using both a T-D-S and Shake Flask system. The inoculum was prepared from a 14-day die away test.
Result	:	Primary biodegradation was determined to be 67+/- 14 % at the charge rate of 5 mg/24 hr of 97 Adipate and 88+/-5% at a rate of 20 mg/24 hr. ; CO2 evolution in the Ultimate biodegradation study was 90.2% and 78.7-82.1% in the T-D-S and Shake flask methods tested, respectively.

82.1% in the T-D-S and Shake flask methods t ested, respectively.

Test substance : Technical grade 97 Adipate with purity of 99%.

Conclusion : Rapid and essentially complete degradation was observed in both the SCAS and CO2 Evolution tests, indicating rapid degradation by microbial populations in the environment.

Reliability : (1) valid without restriction
OECD Methodology similar to # 302, well documented.

Flag : Critical study for SIDS endpoint

29.05.2003 (8)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	static
Species	:	Oncorhynchus mykiss (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
NOEC	:	> 1000 -
LC0	:	> 1000 -
Limit test	:	
Analytical monitoring	:	no
Method	:	other
Year	:	1980
GLP	:	yes
Test substance	:	other TS
Method	:	Followed methods described in EPA-600/3-75-009, Methods for Acute Toxicity tests with Fish, Macroinvertebrates and Amphibians, 1975. The test treatments were prepared by individually mixing the appropriate amount of test substance with 10 ml of actone and adding it directly to the test chambers. The control also received 10 ml of acetone. One replicate was prepared for each test treatment and control. The test was performed in 5-gallon glass vessels containing 15 L of dilution water. The dilution water was filtered well-water. each treatment vessel contained 10 fish. Fish were obtained from Fenders' Fish Hatchery in Baltic, Ohio and had a mean lenth of 33 mm and weight of 0.43 g. Well water hardness was 225 ppm CaCo3. Light cycle was 16-h light:8-h dark.
Result	:	No mortalities were observed in any of the test concentrations tested, including: control, 100, 180, 320, 560 or 1000 mg/L. thus the LC50 is considered to be > 1000 mg/L. It should be recognized that the test substance was insoluble at all test levels as an oily sheen was seen in each treated vessel. Test temp. was 12+/-1 Deg C.; the pH range was 7.7-7.9 and Dissolved oxygen ranged from 8.6-10 mg/L.
Test substance	:	Technical grade Santicizer 97A with purity of 99%.
Reliability	:	(2) valid with restrictions Study conducted according to well accepted test guidelines which preceeded OECD guidance and was well documented. Established that level of toxicity was above solubility limit (48ppb) of this test agent, although value cited for LC50 is far in excess.
Flag	:	Critical study for SIDS endpoint

29.05.2003 (9)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	static
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC50	:	= 1.9 -
Analytical monitoring	:	no
Method	:	other
Year	:	1980
GLP	:	yes
Test substance	:	other TS
Method	:	Followed methods outlined in USEPA, 660/3-75-009. Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians. 1975. Test treatments were prepared by adding the test substance with 0.2 ml acetone directly to the test treatments. Two replicates of 10 organisms were tested

directly to the test treatments. Two replicates of 10 organisms were tested per treatment. Test vessels were 250 ml beakers with 200 ml of test solution. The dilution water was well water. A moving average angle, Probit or Bionomial method was used for statistical analysis.

Result : An LC50 of 1.9 mg/L with CI of 1.5-2.3 mg/L. Mortality (%) observed at following levels: Control (0%), solvent control (0%), 1 mg/L (0%), 1.8 mg/L (55%), 3.2 mg/L (95%), 5.6 mg/L (85%), 10 mg/L (100%), 18 mg/L (100%). Test substance was observed on the surface of all treatment test vessels. Daphnids were observed trapped in the test substance, which affected immobilization.Test temp. was 20 +/-1 Deg. C., the pH was 7.4 during the study and the Dissolved oxygen was 9.2 mg/L. Water hardness was reported as 225 ppn CaCO3. Daphnia were < 24 hr old and obtained from in-house stock. Lighting was 16 hrs light and 8 hrs dark.

Test substance : Technical grade Santicizer 97A with purity of 99%.

Conclusion : LC50 value above the level of solubility (i.e. < 1mg/L) is unreliable in this test due to test material interference and immobilization of test organisms above 1 mg/L. However, at a test level slightly above the determined level of solubility (1 mg/L) no deaths occurred and thus no interference with test material affected test results. Thus, this study is adequate to judge the lack of toxicity of this test agent at the level of water solubility.

Reliability : (2) valid with restrictions
This study provides adequate information at the level of water solubility, where no toxicity was observed, in a well documented study conducted according to EPA test guidelines established prior to OECD codification of similar guidance.

Flag : Critical study for SIDS endpoint

29.05.2003 (10)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species : Selenastrum capricornutum (Algae)
Endpoint : growth rate
Exposure period : 96 hour(s)
Unit : mg/l
EC50 : = 2.5 -
Limit test :
Analytical monitoring : no
Method : other
Year : 1980
GLP : yes
Test substance : other TS

Method : Followed US EPA Printz Algal Assay Test (1978). A primary stock was prepared by adding the test substance to dimethylformamide (DMF). Secondary stock solutions (test treatments) were then prepared by serial dilution using the primary stock. A solvent control (0.05 ml, max. amount added to any test flask) of DMF was also tested. Algal growth medium was used as the control. Three replicates of each test treatment were tested. The initial algal concentration was 2.0X10E4 cells per ml.Lighting was = 4000 lux; temp. was 24+/-1 Deg. C; the pH range was 7.1-7.2. Used a 24-h light cycle. Algal culture stock was obtained from USEPA Envi ronmental Research Laboratory, Corvallis, Oregon. Statistical methods used: probit, linear regression, Student's t-test for growth differences.Chlorophyll was measured daily using a Turner filter fluorometer. Cell counts were performed via a hemacytometer at study termination.

Result : EC50 (based on cell nos.) = 2.5 ppm; EC50 (based on chlorophyll measurements) = 1.8 ppm; Differences (between test level and control level) seen at 96 h in Chlorophyll: solvent control (0%), 0.3 mg/L (+17%), 0.6 mg/L (-13%), 1.2 mg/L (-56%), 2.5 mg/L (-61%), and 5 mg/L (-70%). Differences in cell no. at similar levels were: solvent control (-1%), 0.3 mg/L (+4%), 0.6 mg/L (-7%), 1.2 mg/L (-47%), 2.5 mg/L (-54%), and 5 mg/L (-

(+4%), 0.6 mg/L (-7%), 1.2 mg/L (-47%), 2.5 mg/L (-54%), and 5 mg/L (-62%).

Test substance : Technical grade Santicizer 97A was 99% pure.

Reliability : (2) valid with restrictions
Provides adequate toxicity information (NOEL < 48 ppb) up to the level of solubility, although EC50 is reportedly higher than the solubility limit.

Flag : Critical study for SIDS endpoint

29.05.2003 (11)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	> 15800 - mg/kg bw
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	10
Vehicle	:	other
Doses	:	
Method	:	other
Year	:	1970
GLP	:	no
Test substance	:	other TS
Method	:	Undiluted test material was fed by stomach tube to rats in increasing doses at increments of fractional log intervals. The dose levels were 2000, 3160, 5010, 7940, 12600 and 15800 mg/kg. Single rats were used for the lower doses while 5 rats (3 male, 2 female) were used at 15800 mg/kg. Daily observations were made for toxic signs and a complete necopsy was performed after 7 days.
Result	:	No animals died at any dose level. Toxic signs reported as reduced appetite and activity for 1-4 days and slight weakness. All rats were considered normal after 7 days. At necropsy, 2/5 rats at 15800 mg/kg were observed with slight congestion of the lungs.
Test substance	:	Santicizer 97A commercial grade >99% pure.
Conclusion	:	Compound considered practically non-toxic by oral ingestion in male and female rats.
Reliability	:	(2) valid with restrictions Conducted pre-GLP, but adequately documented.
Flag	:	Critical study for SIDS endpoint

29.05.2003 (12)

5.1.2 ACUTE INHALATION TOXICITY

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD0
Value	:	> 7940 - mg/kg bw
Species	:	rabbit
Strain	:	New Zealand white
Sex	:	male/female
Number of animals	:	5
Vehicle	:	other
Doses	:	
Method	:	other
Year	:	1970
GLP	:	no
Test substance	:	other TS
Method	:	Undiluted compound was applied in increasing doses at increments of 0.2 fractional log intervals to closely clipped, intact skin of male and female rabbits. Single animals were tested at lower dosages while 1 male and 1

rabbits. Single animals were tested at lower dosages while 1 male and 1 female rabbit were tested at the highest level. The dose levels were 2000, 3160, 5010 and 7940 mg/kg. Treated areas were covered with plastic strips (occluded) and animals held in wooden stocks for 24 hrs before removal. Animals were observed for signs of toxicity for 1 4 days, after which they were necropsied and evaluated for macroscopic lesions.

Result : No deaths were observed in the study. Toxic signs reported were reduced appetite and activity, slight lethargy (2-5 days duration) and slight tremors (1-2 days) at 5010 and 7940 mg/kg. At necropsy, rabbits at 5010 and 7940 mg/kg were observed with slight congestion of the lungs and areas of slight discoloration of the liver.

Test substance : Santicizer 97A commercial grade, > 99% pure.

Conclusion : Compound was considered practically non-toxic by dermal exposure in male and female rabbits.

Reliability : (2) valid with restrictions
Pre-GLP study; provided as Supplemental information.

29.05.2003 (12)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

5.2.2 EYE IRRITATION

5.3 SENSITIZATION

5.4 REPEATED DOSE TOXICITY

Type : Sub-chronic
Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : oral feed
Exposure period : 90 days
Frequency of treatm. : Daily
Post exposure period : None
Doses : 0 (negative control), 0.1, 0.5 and 2.5 %;
Control group : yes, concurrent no treatment
NOAEL : > 2.5 - %
Method : other
Year : 1972
GLP : no
Test substance : other TS

Method : Methodology consistent with OECD 408 but preceeded codification. Groups of 15 male and 15 female rats were administered diets containing test substance at 0, 0.1, 0.5 or 2.5% for 13 weeks. The high dose male rats received approx. 1500 mg/kg/d and females received 1900 mg/kg/d. A comparative group of 15 rats/sex were given 2.5% dioctyl adipate. Body weights (15/sex/group) and food consumption (5/sex/group) were measured weekly. Individual animal observations were recorded daily and detailed exams performed weekly. No ophthalmoscopic exam was performed. Hematology (Hgb, Hct, RBC, Total and differential leukocytes), clinical blood chemistry (SAP, BUN, SGPT, fasting blood glucose) and urine analysis (Glu, Alb, pH, specific gravity, microscopic elements) were

urine analysis (Glu, Alb, pH, specific gravity, microscopic elements) were performed on 10 rats/sex/group from the untreated control group, the high dose test group and the DOA test group after 45 and 84 days on test. Absolute and relative organ weights were recorded for liver, kidney, spleen, gonads, heart and brain at study termination. After 90 days, each rat was necropsied. A complete set of approx. 40 tissues (esophagus, stomach-3 areas, small intestine-3 sections, cecum, colon, liver, kidneys, spleen, pancreas, urinary bladder, pituitary, adrenal, testes, seminal vesicles, ovary, b. marrow, thyroid, parathyroid, salivary gland, prostate, heart, aorta, lung, lymph nodes (2), skeletal muscle, peripheral nerve, femur, spinal cord, uterus, trachea, eye, optic nerve, and brain-3 sections) was examined from 10 rats/sex from the untreated control group, the high dose test group, and the DOA group. Mean body weight, food consumption and organ weight values were evaluated by analysis of variance (ANOVA) and significant differences among the groups were examined by t-test. A level of $p<0.05$ was used to determine significance.

Result : Three deaths occurred during the study and were attributed to an acute respiratory infection. There were no differences noted between the untreated control and any of the Di (C7-C9 alkyl) adipate test groups for body weights, food consumption, or blood or urine parameters. Small but significantly Increased absolute and relative kidney weights were noted for females, but not males, in the high dose group. These findings were not considered treatment-related based on the small changes seen only in females without corresponding clinical or microscopic parameters which would be indicative of a renal effect. Necropsy findings were considered spontaneous and not test substance-related. The most frequent findings in all groups were lesions in the trachea and lungs consistent with chronic infection. No weight changes nor microscopic findings indicative of a treat-related effect were observed in gonads from either sex. Dioctyl adipate (DOA) exhibited statistically significantly decreased body weight gains (both sexes) and statistically increased female kidney and liver weights and weight ratios.

Test substance : Santicizer 97 commercial grade, > 99% pure.

Reliability : (2) valid with restrictions
Study underwent independent audit and judged to have met Acceptable standard by FDA. Individual data not presented in report.

Flag : Critical study for SIDS endpoint

29.05.2003 (13)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Ames test

System of testing : S. typhimurium strains TA98, TA100, TA1535 and TA1537

Test concentration : 0.0, 0.01, 0.04, 0.2, 1.0, 3.0, and 10.0 uL/plate and 25 uL/spot in spot test

Cycotoxic concentr. : none observed at highest dose tested of 10 uL/plate in plate incorporation assay

Metabolic activation : with and without

Result : negative

Method : OECD Guide-line 471

Year : 1981

GLP : yes

Test substance : other TS

Method : Positive control chemicals were sodium nitrite, benzo(a)pyrene, 2-nitrofluorene, 9-aminoacridine and 2-aminoanthracene; the solvent control was ethanol. Concurrent solvent and positive controls were included in all experiments and performed as expected. A toxicity pretest with TA 100 was conducted with and without microsomal activation to determine cytotoxicity and identify the highest dose level to be used in the full study. Both plate incorporation and spot tests were conducted in triplicate in all

strains with and without activation. A mutagenic response was defined as a reproducible, dose-related increase in the number of histidine-independent colonies over the spontaneous incidence. Bartlett's test was run to determine whether significant differences existed among treatment variables. Treatment groups were compared to solvent control using a 1-sided t-test and within level pooled variance. Dose response was further evaluated for all treatment groups found to be significantly ($p<0.01$) higher than solvent control.

Result : The substance was not mutagenic at doses up to 10 uL/plate in Salmonella strains TA 98, TA 100, TA 1535 and TA 1537 in the plate incorporation assay nor at 25 uL/spot in the spot test with or without metabolic activation. No microbial toxicity was observed in strain TA1 00 at concentrations up to 10 uL/plate in plate incorporation assay nor at 25 uL/spot in the spot test with or without metabolic activation. Decreased solubility was observed at 3 and 10 uL in the plate incorporation assay.

Test substance : Santicizer 97 commercial grade, > 99% pure.

Conclusion : The test substance was not mutagenic in all strains tested.

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

29.05.2003 (14)

Type : Mouse lymphoma assay

System of testing : L5178Y Mouse Lymphoma cell line heterozygous at the thymidine kinase (TK) locus

Test concentration : without S9: 50, 200, 500, 1000, 1500, 2010, 2490 & 3000 ug/ml; with S9: 520,1000, 1520, 2000, 2520, 3000, 3520 & 4000 ug/ml

Cycotoxic concentr. : without S9: 500 ug/ml and higher; with S9: 4000 ug/ml 62% mean rel. growth rate, and 520 ug/ml growth rate reduced to 81%.

Metabolic activation : with and without

Result : negative

Method : OECD Guide-line 476

Year : 1982

GLP : yes

Test substance : other TS

Method : L5178Y mouse lymphoma cells, heterozygous for thymidine kinase, were used as target cells and were grown in a suspension culture in F10P medium. Cells (6 x 10E6) in medium were prepared in centrifuge tubes and exposed to the test or control agent, with our without the addition of a metabolic activation system (S9). S9 liver homogenate was prepared from F-344 male rats pretreated with Arochlor 1254. A solvent control (dimethyl sulfoxide) was also run. Positive controls consisted of: ethyl methanesulfonate and 3-methylcholanthrene. All test concentrations were run in triplicate. Test material was diluted in dimethyl sulfoxide. Tubes were rotated for 4 hrs at 37 deg. C and treatment solutions removed from the cells by centrifugation. Cells were resuspended in fresh medium. Cells were suspended in 15 ml medium for a final density of 4 x 10E5 cells/ml CO2 flushed and then rotated during a 2 day expression period. After the expression period, cells were seeded in soft agar medium and cultivated for 11 days in an atmosphere containing CO2. Colonies of cells formed in each petri dish were counted using an automatic colony counter. A concentration range-finding assay was run to determine the cytotoxicity of the test compound and to determine the concentration range to use in the mutagenesis assays. Final test concentratons for the mutagenicity study were: without S9: 50, 200, 500, 1000, 1500, 2010, 2490 & 3000 ug/ml; with S9: 520,1000, 1520, 2000, 2520, 3000, 3520 & 4000 ug/ml. Mutation frequency was calculated by dividing the number of mutant colonies by the number of potentially viable colonies per 3 x 10E6 cells plated. The number of potentially viable colonies was calculated by multiplying the 3 x 10E6 cells plated by their specific plating efficiency. Induced mutation frequencies were calculated by subtraction of solvent control mutant frequency mean values from each treated sample. Transformed data were analyzed statistically using the 1-tailed Student's t-test and the dose-

analyzed statistically using the 1-tailed Student's t-test and the dose-response analysis of variance generally by Irr and Snee (1981). Data from the tests with and without the S9 fractions were analyzed separately. In all cases, p< 0.01.

Remark : Supplemental information for HPV program.

Result : Without S9: Test article most toxic at 3000 ug/ml, yielding a mean relative total growth value of 20.1%. No significant depression in the relative total growth value was observed at or below 200 ug/ml. None of the mean mutation frequencies of tested concentrations was significantly greater than that of the solvent control. The linear component of the concentration dose-response was not statistically significant.

With S9: Test article was somewhat toxic (61.9% mean relative total growth value) at 4000 ug/ml. The lowest concentration tested, 520 ug/ml, yielded a mean relative total growth value of 81.1%. None of the tested concentrations yielded mean mutation frequencies significantly greater than that of the solvent control. The linear component of the dose-response relationship was not statistically significant.

Test substance : Commercial grade Santicizer 97, purity of 99%.

Reliability : (1) valid without restriction

29.05.2003 (15)

5.6 GENETIC TOXICITY 'IN VIVO'

5.7 CARCINOGENICITY

5.8.1 TOXICITY TO FERTILITY

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	rat
Sex	:	female
Strain	:	Sprague-Dawley
Route of admin.	:	gavage
Exposure period	:	Gestation days 6-19
Frequency of treatm.	:	Daily during the gestation period
Duration of test	:	Animals were sacrificed on gestation day 20
Doses	:	0, 1000, 4000 and 7000 mg/kg/d
Control group	:	yes, concurrent vehicle
NOAEL maternal tox.	:	>= 4000 - mg/kg bw
NOAEL teratogen.	:	>= 7000 - mg/kg bw
NOAEL Embryotoxicity	:	>= 4000 - mg/kg bw
NOAEL Fetotoxicity	:	>= 4000 - mg/kg bw
Method	:	OECD Guide-line 414 "Teratogenicity"
Year	:	1981
GLP	:	yes
Test substance	:	other TS

Method : Females were cohabited overnight with males in a 2:1 ratio. Gestation day 0 was determined the morning that vaginal sperm or plug was found. Mated females were assigned to groups to achieve 24/group. Female rats were dosed daily on Days 6-19 of gestation. Body weights were recorded on GD 0, 6, 15 and 20. Individual clinical observations were recorded on GD 0, 6, 10, 15 and 20. Animals were sacrificed on GD 20 and intact uteri were removed and weighed. All fetuses were weighed and examined for

		external abnormalities; approximately one half were processed for skeletal examination and one half preserved for soft tissue examination. Mean data was analyzed using analysis of variance (ANOVA). Bartlett's test was used to test for equal variance and Dunnett's test for differences from control For incidence data, a Chi-square analysis and Fisher's Exact Probability test were used, followed by Armitage's test for linear trend, if needed.
Result	:	No dams died during the study. Significant maternal body weight decreases ($p<0.01$) were observed at 7000 mg/kg/d (mean of 277 g. vs control of 297 g.) There were no significant differences in the number of implantations, live fetuses, resorptions or corpea lutea. There were no statistically significant effects on mean fetal body weight or sex ratio. High dose (7000 mg/kg) male and female fetal weights were slightly (males= 3.66g vs 3.83g; females = 3.55 vs 3.65), but not statistically, reduced from the control, low (males=3.78; females= 3.63) and mid dose (males=3.79; females=3.63) groups. There were no differences among groups for fetal ossification variations, external, visceral or skeletal malformations. A higher incidence of rudimentary structures (unilateral or bilateral and adjacent to the last thoracic or first lumbar vertebral transverse process) was observed in high dose fetuses (frequency of 35; 28% pups affected) when compared to controls (19;12.4%), low dose (16, 10.7%) or mid dose (20; 13.4%) but were within the range (lab mean of 15.3% with range of 1.9 -33.3% from 17 studies over 4 yrs previous) of historical controls at this laboratory.
Test substance	:	Santicizer 97 commercial grade, > 99% pure.
Conclusion	:	No evidence of developmental toxicity was observed at dose levels of 1000 and 4000 mg/kg/day. Maternal toxicity (reduced body weight) and embryotoxicity (reduced fetal weight) was observed at the highest dose (7000 mg/kd/d) tested.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

29.05.2003 (16)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

Type	:	other
In vitro/in vivo	:	In vivo
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	oral feed
Exposure period	:	91 days
Frequency of treatm.	:	daily
Duration of test	:	90 days
Doses	:	0.1%, 0.5% and 2.5% diet
Control group	:	yes, concurrent vehicle
Result	:	No effects seen on organ weights, organ:body weight ratio, or histopathology for testes or ovaries from any test level.
Method	:	other: study reported in repeated dose section
Year	:	1971
GLP	:	no
Test substance	:	other TS
Remark	:	Supplementary information.
Test substance	:	Commercial grade Santicizer 97.
Reliability	:	(1) valid without restriction

29.05.2003 (13)

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

5.11 ADDITIONAL REMARKS

6.1 ANALYTICAL METHODS

6.2 DETECTION AND IDENTIFICATION

7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

8.1 METHODS HANDLING AND STORING

8.2 FIRE GUIDANCE

8.3 EMERGENCY MEASURES

8.4 POSSIB. OF RENDERING SUBST. HARMLESS

8.5 WASTE MANAGEMENT

8.6 SIDE-EFFECTS DETECTION

8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER

8.8 REACTIVITY TOWARDS CONTAINER MATERIAL

(1) Verschueren, K. 2001. Handbook of Environmental Data on Organic Chemicals. 4th edition, Vol 1:975. John Wiley & Sons, Inc. New York.

(2) Kern, J and JR Darby, The Technology of Plasticizers. Wiley, 1982

(3) Solutia study no. ES-80-SS-41. 1980. Octanol/Water Partition Coefficient of SANTICIZER 97A and Dioctyl Adipate.

(4) Solutia study no. MO20020442. 1982. Aqueous solubility of Santicizer 97.

(5) Solutia Study no. MO19820071. 1981. Sunlight photolysis screening of Santicizer 97.

(6) AOPWIN. Version 1.90. Atmospheric Oxidation. EPIWIN. Version 3.05. 2002. Syracuse Research Corporation, Syracuse, NY.

(7) EPIWIN, version 3.10. 2002. Syracuse Research Corp., Syracuse, NY.

(8) Saeger, VW, RG Kaley II, O Hicks, ES Tucker and JP Mieure. 1976. Appl Environ Microbiol. 31 (5):746-749.

(9) Solutia Study no. AB19800352. 1980. Acute toxicity of S-97A to Rainbow Trout.

(10) Solutia Study no. AB19800354. 1980. Acute toxicity of Santicizer 97A to Daphnia magna.

(11) Solutia Study no. BN19800355. 1980. Toxicity of Santicizer 97A to the freshwater algae Selenstrum capricornatum.

(12) Solutia Study no. Y-70-112. 1970. Acute Toxicological Investigation of Santicizer 97A [EPA Document no. 88-920007905]

(13) Solutia study no. BT-71-38. 1972. 90-Day subacute oral toxicity study with Santicizer 97 in albino rats.

(14) Solutia Study no. DA-80-503. 1981. Salmonella Mutagenicity Assay of Santicizer 97.

(15) Solutia Study No. SR-80-532. 1982. An evaluation of mutagenic potential of Santicizer 97 employing the L5178Y TK =/- Mouse Lymphoma Assay.

(16) Solutia Study no. BD-81-131. 1981. Teratogenicity study in rats with Santicizer 97.

10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT